



Invited Commentary | Pediatrics

Young Women and Oral Human Papillomavirus— Vaccination Is Associated With Protection

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The study by Schlecht et al¹ of adolescent girls and young women answers 4 important questions. First, do sexually active adolescent girls and young women have detectable oral human papillomavirus (HPV)? Second, if so, how long does it take for oral HPV to be cleared? Third, is oral HPV associated with HPV in other anatomic sites? Fourth, in this population, is vaccination with the quadrivalent HPV vaccine associated with reduced prevalence of oral HPV? The authors found that, yes, the study participants who attended an urban, free adolescent clinic had oral HPV, because 6.2% of their oral rinses had HPV types that can cause mucosal infections. Second, the participants overall quickly cleared their incident oral HPV. Third, detectable cervical HPV was associated with oral HPV, linking HPV at the cervix as an indicator of future detection of HPV in the oral cavity. Fourth, and most significant, if the participants had received at least 1 dose of the quadrivalent HPV vaccine, they had a lower risk of oral HPV than those who were fully unvaccinated.

These findings are important to examine more closely. The oral HPV prevalence rate reported by Schlecht et al¹ matches recent data for oral rinses in adults² and demonstrates that their participants' exposure rates to HPV were typical of large clinical cohorts, and not unique to a single urban clinic site. Also, when incident detection of oral HPV did occur, the participants were able to clear it quickly. Almost none had oral HPV that remained for more than 12 months, and this trend also prevailed longitudinally. When determined according to years since first sexual activity, the longer a participant had been sexually active, the lower her odds of having oral HPV detected.

With regard to the data on vaccine efficacy in this cohort,¹ the association was strong. There have been multiple studies^{3,4} in adolescents who received the 3-dose HPV vaccine that demonstrate high-titer antibody responses to the HPV types included in the vaccine³ and clinical protection against infection at anogenital sites.⁴ However, to our knowledge, no other study to date has looked at the association between vaccination and clinical protection against HPV infection the oral cavity, specifically in minority girls and young women. This makes the findings of Schlecht et al¹ even more critical. Participants in this study who were vaccinated had fewer episodes of incident oral HPV DNA.

Adding to the robustness of this finding is that these data extend from participants who mirror an intention-to-treat, rather than a per-protocol, cohort in clinical trials. First, participants were not excluded if they had not completed the full 3-dose series (which was the standard recommendation when they were enrolled). Instead, Schlecht et al¹ considered their participants as vaccinated if they had received at least 1 dose. Recent research⁵ has shown that 2 doses, or even 1, of the HPV vaccine can mount type-specific titers to HPV and are associated with a decreased risk of HPV infection and disease. The study by Schlecht et al¹ expands that association to oral HPV protection as well. Second, participants were not excluded if they had not received their vaccine series before becoming sexually active. The data demonstrating protection from oral HPV may be even more robust among adolescents who received 1 or more vaccination dose before exposure through sexual activity, and it would be very interesting to determine whether those who had oral HPV detected had been vaccinated before they became sexually active.

Schlecht et al¹ did an excellent job collecting sexual histories from their participants. Knowing where anatomically someone has been exposed to HPV, and the timing of that exposure, is critical to understanding the natural history and clearance rates of an infection. It is also important to understand whether HPV infections in 1 anatomic site can be associated with infection at other sites.

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Other studies⁶⁻⁸ have shown these links between cervical and anal infections and disease, and now the study by Schlecht et al¹ associates cervical HPV detection with oral HPV detection, although not yet with disease.

Few prevalence or prevention data on oral HPV have been collected among minority adolescents, especially those who live in urban areas, making the study by Schlecht et al¹ very important. However, there are limitations that should be noted. First, the study was conducted at a single clinical site. Future studies at multiple sites, and among different socioeconomic cohorts of participants, will add robustness to the data on oral HPV. Second, nearly all participants in the study had received at least 1 dose of the quadrivalent HPV vaccine. Only 15% had not. This is laudable for the clinic, having been able to administer the HPV vaccine to a cohort that many would consider to be high risk behaviorally and socioeconomically. However, the comparison group of participants, nonvaccinated vs vaccinated, is not equal in size, and the size discrepancy also limits the power to detect important risk factors for HPV acquisition. In addition, there may be some associated risk factor among minority adolescents and young adults who attend a free clinic, and yet do not receive an offered vaccine, that leads to increased oral HPV prevalence. This should be further studied.

The most important limitation in this study's findings is that it is of girls and women only. The risk of HPV-associated head and neck squamous cell carcinoma is much higher among men than among women; some estimates are that, for every woman, 2 to 5 men receive a diagnosis.^{9,10} With that in mind, we do not know the oral incidence, prevalence, and clearance of HPV in adolescent boys and young men in general, let alone those who are part of a minority group. The National Health and Nutrition Examination Survey data² show greater HPV DNA prevalence among men vs women, and this increases with the number of lifetime partners. Do men have a greater risk of oral HPV acquisition or a poorer clearance of infection? Is exposure greater for a man who has sex with women vs a man who has sex with men? Males may be a challenging group to study, but these are critical questions that currently remain unanswered. The data presented in the study by Schlecht et al,¹ however, lay the groundwork to study HPV in males and, if similar findings are noted, provide yet another reason to vaccinate adolescent boys and young men against HPV.

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